

10/544093

SEQUENCE LISTING

<110> Yednock, Ted
Vasquez, Nicki
Bard, Frederique
Seubert, Peter A.

<120> ACTIVE IMMUNIZATION TO GENERATE ANTIBODIES TO SOLUBLE A-BETA FOR
PREVENTION AND TREATMENT OF AMYLOIDOGENIC DISEASE

<130> 15270J-009820US

<140> US 10/544,093

<141> 2004-01-31

<150> WO PCT/US2004/002856

<151> 2004-01-31

<150> US 60/444,150

<151> 2003-02-01

<160> 27

<170> PatentIn version 3.2

<210> 1

<211> 42

<212> PRT

<213> Homo sapiens

<400> 1

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala
35 40

<210> 2

<211> 5

<212> PRT

<213> Artificial

<220>

<223> Reversomer of A-beta 1-5

<400> 2

Arg Phe Glu Ala Asp
1 5

<210> 3

<211> 17

<212> PRT

<213> Artificial

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<223> Artificial peptide derived from residues 323-339 of ovalbumin.

<400> 3

Ile	Ser	Gln	Ala	Val	His	Ala	Ala	His	Ala	Glu	Ile	Asn	Glu	Ala	Gly
1				5					10					15	

Arg

<210> 4

<211> 16

<212> PRT

<213> Plasmodium sp.

<400> 4

Glu	Lys	Lys	Ile	Ala	Lys	Met	Glu	Lys	Ala	Ser	Ser	Val	Phe	Asn	Val
1				5					10					15	

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<212> PRT

<213> Hepatitis B virus

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Phe	Phe	Leu	Leu	Thr	Arg	Ile	Leu	Thr	Ile
1				5					10

<210> 6

<211> 19

<212> PRT

<213> Artificial

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<223> Heat Shock Protein 65 fragment

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Asp	Gln	Ser	Ile	Gly	Asp	Leu	Ile	Ala	Glu	Ala	Met	Asp	Lys	Val	Gly
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Asn Glu Gly

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<211> 14

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<223> Bacille Calmette-Guerin fragment

<400> 7

Gln Val His Phe Gln Pro Leu Pro Pro Ala Val Val Lys Leu
1 5 10

<210> 8

<211> 15

<212> PRT

<213> Clostridium tetani

<400> 8

Gln Tyr Ile Lys Ala Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu
1 5 10 15

<210> 9

<211> 21

<212> PRT

<213> Clostridium tetani

<400> 9

Phe Asn Asn Phe Thr Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser
1 5 10 15

Ala Ser His Leu Glu
20

<210> 10

<211> 16

<212> PRT

<213> Human immunodeficiency virus

<400> 10

Lys Gln Ile Ile Asn Met Trp Gln Glu Val Gly Lys Ala Met Tyr Ala
1 5 10 15

<210> 11

<211> 13

<212> PRT

<213> Artificial

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<223> PADRE peptide

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<223> X is cyclohexylalanine, tyrosine, or phenylalanine.

<400> 11

Ala Lys Xaa Val Ala Ala Trp Thr Leu Lys Ala Ala Ala
 1 5 10

<210> 12
 <211> 58
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 <213> Artificial

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 <223> Only a contiguous fragment of residues 1-43 are present.
 Preferred fragments are 5-10 or 7-10 residues in length.

<400> 12

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Gln Tyr Ile Lys Ala
 35 40 45

Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu
 50 55

<210> 13
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 <223> Only a contiguous fragment of residues 1-43 are present.
 Preferred fragments are 5-10 or 7-10 residues in length.

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Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Phe Asn Asn Phe Thr
 35 40 45

Val Ser Phe Trp Leu Arg Val Pro Lys Val Ser Ala Ser His Leu Glu
 50 55 60

<210> 14
 <211> 58
 <212> PRT
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<220>
 <223> A-beta fragment-tetanus toxoid fusion protein

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 Preferred fragments are 5-10 or 7-10 residues in length.

<400> 14

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Gln Tyr Ile Lys Ala
 35 40 45

Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu
 50 55

<210> 15
 <211> 79
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 <213> Artificial

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 <223> A-beta fragment tetanus-toxoid fusion protein

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 Preferred fragments are 5-10 or 7-10 residues in length.

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 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Gln Tyr Ile Lys Ala
 35 40 45

Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu Phe Asn Asn Phe Thr Val
 50 55 60

Ser Phe Trp Leu Arg Val Pro Lys Val Ser Ala Ser His Leu Glu
 65 70 75

<210> 16
 <211> 56
 <212> PRT
 <213> Artificial

<220>
 <223> Padre-A-beta fragment fusion protein

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 <222> (3)..(3)
 <223> X is cyclohexylalanine, tyrosine, or phenylalanine.

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 Preferred fragments are 5-10 or 7-10 residues in length.

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Ala Lys Xaa Val Ala Ala Trp Thr Leu Lys Ala Ala Ala Asp Ala Glu
 1 5 10 15

Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe
 20 25 30

Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met
 35 40 45

Val Gly Gly Val Val Ile Ala Thr
 50 55

<210> 17
 <211> 142
 <212> PRT
 <213> Artificial

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<220>
<223>  A-beta-A-beta-A-beta-Padre fusion protein

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        Preferred fragments are 5-10 or 7-10 residues in length.

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<221>  MISC_FEATURE
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<223>  Only a contiguous fragment of residues 44-86 are present.
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<220>
<221>  MISC_FEATURE
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<223>  Only a contiguous fragment of residues 87-129 are present.
        Preferred fragments are 5-10 or 7-10 residues in length.

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<400>  17

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
1          5          10          15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
          20          25          30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg
          35          40          45

His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala
          50          55          60

Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly
65          70          75          80

Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly Tyr
          85          90          95

Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser
          100          105          110

Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala
          115          120          125

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Thr Ala Lys Xaa Val Ala Ala Trp Thr Leu Lys Ala Ala Ala
 130 135 140

<210> 18
 <211> 185
 <212> PRT
 <213> Artificial

<220>
 <223> Fusion protein

<220>
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Ala Lys Xaa Val Ala Ala Trp Thr Leu Lys Ala Ala Ala Asp Ala Glu
 1 5 10 15

Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe
 20 25 30

Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met
 35 40 45

Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser
 50 55 60

Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val

65 70 75 80
 Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val
 85 90 95
 Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His
 100 105 110
 His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly
 115 120 125
 Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Asp Ala
 130 135 140
 Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val
 145 150 155 160
 Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu
 165 170 175
 Met Val Gly Gly Val Val Ile Ala Thr
 180 185

<210> 19
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<400> 19

Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys
 1 5 10 15
 Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Ala Lys Xaa Val Ala
 35 40 45

Ala Trp Thr Leu Lys Ala Ala Ala
 50 55

<210> 20
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 Preferred fragments are 5-10 or 7-10 residues in length.

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Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Ile Ser Gln Ala Val
 35 40 45

His Ala Ala His Ala Glu Ile Asn Glu Ala Gly Arg
 50 55 60

<210> 21
 <211> 142
 <212> PRT
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<220>
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Preferred fragments are 5-10 or 7-10 residues in length.

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Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys Leu Ala Thr Asp Ala Glu
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20 25 30

Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met
35 40 45

Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser
50 55 60

Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val
65 70 75 80

Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val
85 90 95

Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His
100 105 110

His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly
115 120 125

Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr
130 135 140

<210> 22

<211> 99

<212> PRT

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 Preferred fragments are 5-10 or 7-10 residues in length.

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 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Pro Lys Tyr Val Lys
 35 40 45

Gln Asn Thr Leu Lys Leu Ala Thr Asp Ala Glu Phe Arg His Asp Ser
 50 55 60

Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val
 65 70 75 80

Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val
 85 90 95

Ile Ala Thr

<210> 23
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 <223> Only a contiguous fragment of residues 44-86 are present.
 Preferred fragments are 5-10 or 7-10 residues in length.

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<222> (87)..(129)
 <223> Only a contiguous fragment of residues 87-129 are present.
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<400> 23

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 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg
 35 40 45

His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala
 50 55 60

Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly
 65 70 75 80

Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly Tyr
 85 90 95

Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser
 100 105 110

Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala
 115 120 125

Thr Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys Leu Ala Thr
 130 135 140

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Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg
35 40 45

His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala
50 55 60

Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly
65 70 75 80

Gly Val Val Ile Ala Thr Pro Lys Tyr Val Lys Gln Asn Thr Leu Lys
85 90 95

Leu Ala Thr

<210> 25

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Preferred fragments are 5-10 or 7-10 residues in length.

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 1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Pro Lys Tyr Val Lys
 35 40 45

Gln Asn Thr Leu Lys Leu Ala Thr Glu Lys Lys Ile Ala Lys Met Glu
 50 55 60

Lys Ala Ser Ser Val Phe Asn Val Gln Tyr Ile Lys Ala Asn Ser Lys
 65 70 75 80

Phe Ile Gly Ile Thr Glu Leu Phe Asn Asn Phe Thr Val Ser Phe Trp
 85 90 95

Leu Arg Val Pro Lys Val Ser Ala Ser His Leu Glu Asp Ala Glu Phe
 100 105 110

Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe Phe
 115 120 125

Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val
 130 135 140

Gly Gly Val Val Ile Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly
 145 150 155 160

Tyr Glu Val His His Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly
 165 170 175

Ser Asn Lys Gly Ala Ile Ile Gly Leu Met Val Gly Gly Val Val Ile
 180 185 190

Ala Thr Asp Ala Glu Phe Arg His Asp Ser Gly Tyr Glu Val His His

195		200		205
Gln Lys Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala				
210		215		220
Ile Ile Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Asp Ala Glu				
225		230		235 240
Phe Arg His Asp Ser Gly Tyr Glu Val His His Gln Lys Leu Val Phe				
	245		250	255
Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met				
	260		265	270
Val Gly Gly Val Val Ile Ala Thr Gln Tyr Ile Lys Ala Asn Ser Lys				
	275		280	285
Phe Ile Gly Ile Thr Glu Leu Phe Asn Asn Phe Thr Val Ser Phe Trp				
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Leu Arg Val Pro Lys Val Ser Ala Ser His Leu Glu				
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<210> 26
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 Preferred fragments are 5-10 or 7-10 residues in length.

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 Preferred fragments are 5-10 or 7-10 residues in length.

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			20					25					30		
Gly	Leu	Met	Val	Gly	Gly	Val	Val	Ile	Ala	Thr	Gln	Tyr	Ile	Lys	Ala
		35					40					45			
Asn	Ser	Lys	Phe	Ile	Gly	Ile	Thr	Glu	Leu	Cys	Phe	Asn	Asn	Phe	Thr
	50					55					60				
Val	Ser	Phe	Trp	Leu	Arg	Val	Pro	Lys	Val	Ser	Ala	Ser	His	Leu	Glu
65					70					75					80
Asp	Ala	Glu	Phe	Arg	His	Asp	Ser	Gly	Tyr	Glu	Val	His	His	Gln	Lys
				85					90					95	
Leu	Val	Phe	Phe	Ala	Glu	Asp	Val	Gly	Ser	Asn	Lys	Gly	Ala	Ile	Ile
			100					105					110		
Gly	Leu	Met	Val	Gly	Gly	Val	Val	Ile	Ala	Thr	Gln	Tyr	Ile	Lys	Ala
		115					120					125			
Asn	Ser	Lys	Phe	Ile	Gly	Ile	Thr	Glu	Leu	Cys	Phe	Asn	Asn	Phe	Thr
	130					135					140				
Val	Ser	Phe	Trp	Leu	Arg	Val	Pro	Lys	Val	Ser	Ala	Ser	His	Leu	Glu
145					150					155					160
Asp	Ala	Glu	Phe	Arg	His	Asp	Ser	Gly	Tyr	Glu	Val	His	His	Gln	Lys
				165					170					175	
Leu	Val	Phe	Phe	Ala	Glu	Asp	Val	Gly	Ser	Asn	Lys	Gly	Ala	Ile	Ile
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Gly	Leu	Met	Val	Gly	Gly	Val	Val	Ile	Ala	Thr					
		195					200								

<210> 27
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<223> Only a contiguous fragment of residues 1-43 are present.
Preferred fragments are 5-10 or 7-10 residues in length.

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1 5 10 15

Leu Val Phe Phe Ala Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile
 20 25 30

Gly Leu Met Val Gly Gly Val Val Ile Ala Thr Gln Tyr Ile Lys Ala
 35 40 45

Asn Ser Lys Phe Ile Gly Ile Thr Glu Leu
 50 55